

Notice of Allowability

Application No.

09/927,084

Examiner

JaNa Hines

Applicant(s)

TENNE ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to April 15, 2008.
2. ☒ The allowed claim(s) is/are 64, 65 and 67-83.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>June 10, 2008</u> . |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>4/3/02</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

DETAILED ACTION

Amendment Entry

1. The amendment filed April 15, 2008 has been entered. Claims 42-63 have been cancelled. Claims 1-41 are withdrawn. Claims 64-83 have been newly added.

EXAMINER'S AMENDMENT

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Janet Cord on June 10, 2008.

The application has been amended as follows:

Claims 1-41 are cancelled.

Claim 64 (Currently Amended) A method for diagnosis of malignant neoplasms derived from epithelial tissue cells ~~cancer~~ in a subject comprising the steps of:

- (i) providing at least a first and second fecal sample from said subject;
- (ii) treating said fecal samples to obtain feces-derived bacteria samples;
- (iii) identifying in the feces-derived bacteria samples one or more types of bacteria;
- (iv) determining for each of said one or more types of bacteria its relative fraction from a total count of bacteria in one of the feces-derived bacteria samples;
- (v) isolating one or more types of bacteria from one or both of the feces-derived bacteria samples;

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(vi) preparing a diagnostic sample containing bacteria of the one or more types isolated in step (v), the fraction of each of the one or more types of bacteria in said diagnostic sample corresponding to the relative fraction thereof in the fecal samples, as determined in step (iv);

(vii) interacting said diagnostic sample with ~~cancer~~ cells for a time period sufficient to detect lysis of said ~~cancer~~ cells by said ~~diagnostic sample~~, thereby determining for said fecal sample a tumor cell necrosis index (TCNI) with the following equation:

$$(a-b)/a \times 100 = C$$

wherein C = the tumor cell necrosis index (TCNI)

a = the number of cells in the negative control samples (without the bacteria) or the number of standard cells destroyed in the presence of the control bacteria;

b = the number of cells not destroyed by the tested sample; and

(viii) diagnosing said subject as having or not having a malignant neoplasms derived from epithelial tissue cells ~~cancer~~ in accordance with the TCNI value determined in step (vii).

Claim 65. *(Currently Amended)* A method for diagnosis of malignant neoplasms derived from epithelial tissue cells ~~cancer~~ in a subject comprising the steps of:

(i) providing at least a first and second fecal sample from said subject;

(ii) treating said fecal samples to obtain feces-derived bacteria samples;

(iii) identifying in the feces-derived bacteria samples more than one type of bacteria;

(iv) determining for each of said more than one type of bacteria its relative fraction from a total count of bacteria in one of the feces-derived bacteria samples;

(v) isolating one or more types of bacteria from said one of the feces-derived bacteria samples;

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(vi) preparing a diagnostic sample containing the bacteria isolated in step (v), the fraction of each of the more than one type of bacteria in said diagnostic sample corresponding to the relative fraction thereof as determined in step (iv);

(vii) interacting said diagnostic sample with ~~cancer~~ cells for a time period sufficient to detect lysis of said ~~cancer~~ cells ~~by said diagnostic sample~~, thereby determining for said fecal sample a tumor cell necrosis index (TCNI)) with the following equation:

$$(a-b)/a \times 100 = C$$

wherein C = the tumor cell necrosis index (TCNI)

a = the number of cells in the negative control samples (without the bacteria) or the number of standard cells destroyed in the presence of the control bacteria;

b = the number of cells not destroyed by the tested sample; and

(viii) diagnosing said subject as having or not having a malignant neoplasms derived from epithelial tissue cells ~~cancer~~ in accordance with the TCNI value determined in step (vii).

Claim 66 (Cancelled)

Claim. 67. (Currently Amended) The method of Claim ~~64~~ 66, wherein said feces-derived bacteria are selected from the group consisting of Escherichia, coli, Streptococcus ~~Streptococcus~~ Bois, and Enterococcus ~~sp~~ or a mixture thereof.

Claim 73. (Currently Amended) The method of Claim 72, wherein said Gram-negative anaerobic bacteria is of a genus selected from the group consisting of Escherichia, Salmonella, Shigella, Klebsiella, Yersinia, Enterobacter, Haemophilus, Gardnerella and Pasteurella ~~Escherichia, Salmonella, Shigella, Klebsiella, Yersinia, Enterobacter, Hemophilus, Gardnerella and Pasteurella.~~

Claim 78. (Currently Amended) The method of Claim 77, wherein said Gram-positive bacteria is of a genus selected from the group consisting of Staphylococcus, Enterococcus, Streptococcus, and Lactococcus ~~Staphylococcus, Enterococcus, Streptococcus, and Lactococcus.~~

Claim 79. (Currently Amended) The method of Claim 78, wherein said bacteria is Streptococcus bois or Enterococcus ~~sp. or both.~~

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments and arguments:

- a) The written description rejection of claim 63; and
- b) The rejection of claim 42-59 and 61-63 under 35 U.S.C. 112, second paragraph;

Allowable Subject Matter

4. Claims 64-65 and 67-83 allowed. The claims are free of the prior art but rejected under 112 2nd paragraph. The closest prior art is Karapetian (US Patent 5,344,762) Karapetian teaches a method for the early diagnosis of cancer wherein human feces-derived sample of bacteria is subjected to incubation with a standard culture of cancer cells for a period of time sufficient to enable the interaction between the bacteria and the cancer cells and effecting the determination. However al., Karapetian does not teach or suggest a process a method for diagnosis of malignant neoplasms derived from epithelial tissue cells in a subject comprising the steps of: (i) providing at least a first and second fecal sample from said subject; (ii) treating said fecal samples to obtain feces-derived bacteria samples; (iii) identifying in the feces-derived bacteria samples more than one type of bacteria; (iv) determining for each of said more than one type of bacteria its relative fraction from a total count of bacteria in one of the feces-derived bacteria samples; (v) isolating one or more types of bacteria from said one of the feces-derived bacteria samples; (vi) preparing a diagnostic sample containing the bacteria isolated in step (v), the fraction of each of the more than one type of bacteria in said

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diagnostic sample corresponding to the relative fraction thereof as determined in step (iv); (vii) interacting said diagnostic sample with cells for a time period sufficient to detect lysis of said cells, thereby determining for said fecal sample a tumor cell necrosis index (TCNI)) with the following equation: $(a-b)/a \times 100 = C$ wherein C = the tumor cell necrosis index (TCNI) a = the number of cells in the negative control samples (without the bacteria) or the number of standard cells destroyed in the presence of the control bacteria; b = the number of cells not destroyed by the tested sample; and (viii) diagnosing said subject as having or not having a malignant neoplasms derived from epithelial tissue cells in accordance with the TCNI value determined in step (vii).

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Shanon Foley, can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645